METABOLIC CORRECTION & OPTIMIZATION OF PERIPHERAL NEUROPATHY

"Therapy should be directed at underlying pathogenesis, even when effective symptomatic treatments are available."
— ADA Position Statement[1]

Combination of active B vitamins in peripheral neuropathy[1]
*L-methylfolate, MethylB_{12}, P5P

- Recovery of sensorium
- Neuronal blood flow
- Intraepidermal nerve fiber density

Cofactors directly involved in metabolism of Hcy, an independent risk factor for neuropathy

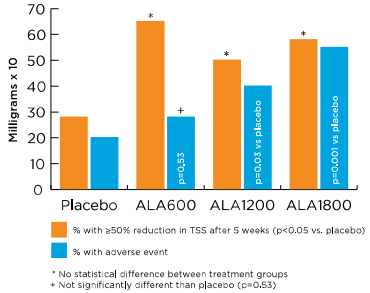
- L-methylfolate
- Vitamin B_{12}
- Vitamin B_6

METHIONINE (amino acid) → HOMOCYSTEINE → CYSTEINE (amino acid)

Sydney 2 Trial: Alpha Lipoic Acid Improves Symptomatic Diabetic Polyneuropathy[2]

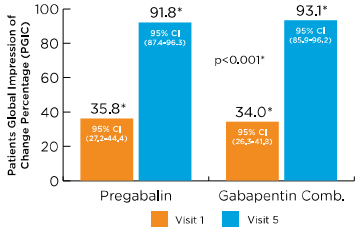
The Sydney 2 Trial examined the effects of alpha-lipoic acid (ALA) on positive sensory symptoms and neuropathic deficits in diabetic patients with distal symmetric polyneuropathy (DSP).

Oral dose of 600mg/d provides optimum risk-to-benefit ratio.



Clinical Trial Assessing the Efficacy of Gabapentin Plus B Complex versus Pregabalin for Painful Diabetic Neuropathy[4]

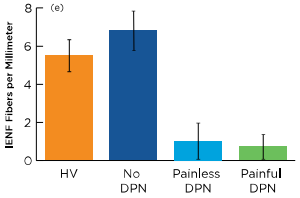
This study shows that GPB Plus B Complex is as effective as PGB with 50% of the gabapentin dose required as monotherapy with less adverse events.



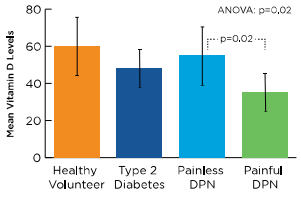
Results show that the GBP plus B Complex is as effective as PGB. *Pain intensity reduction was achieved with a 300 to 1800mg/day dose of GBP/B1/B12 and in the same proportion as PGB 600mg (maximum dose).

Vitamin D Deficiency: An Independent Risk Factor for Diabetic Neuropathy[3]

This study demonstrated a significant difference in vitamin D levels in people with painful diabetic peripheral neuropathy suggesting a possible role for vitamin D in the pathogenesis of painful diabetic peripheral neuropathy.



Both neuropathy groups (Painful and Painless DPN) had significant reduction in IENFD compared to HV (p<0.001).



Significant reduction of Painful-DPN group (p<0.01) and differences between Painful-DPN vs Painless-DPN (p=0.02) and Painful-DPN vs Healthy Volunteers [HV] (p=0.002).

Metformin Leads to Metabolic Deficiency in Diabetic Neuropathy[5-7]

Multiple studies demonstrate metformin exposure may be an iatrogenic cause for exacerbation of peripheral neuropathy in patients with type 2 diabetes.

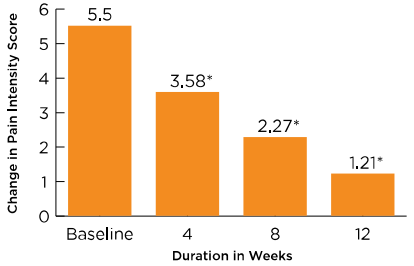
Cumulative metformin dose

- Folate, vitamin B_{12} and vitamin B_1 levels
- Homocysteine levels
- Severity of neuropathy

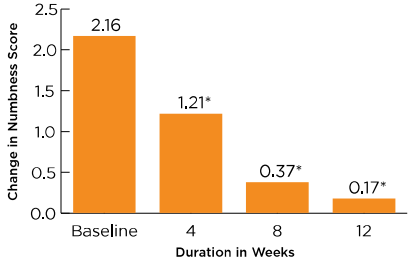
The implications for the metabolic consequences of metformin on Hcy and the risk of neuropathy suggest a role for active folate therapy, especially in patients with some polymorphic variants, including MTHFR.

Fixed Dose Vitamin B Combination and Alpha Lipoic Acid in Diabetic Neuropathy[8]

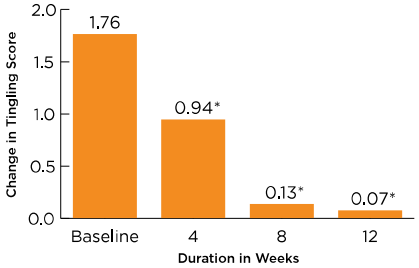
A substantial difference was observed in overall pain intensity, numbness, tingling, and muscle weakness.



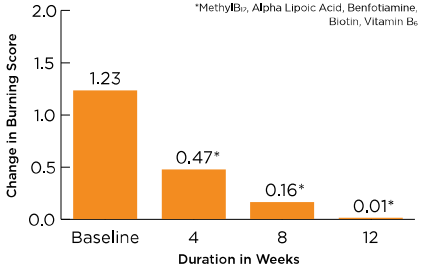
Mean pain score fell 78% after 12 weeks from baseline *p<0.05.



Mean numbness score reduced by 92% after 12 weeks from baseline *p<0.05.



Mean tingling score reduced by 96% after 12 weeks from baseline *p<0.05.



Mean burning score reduced by 99% after 12 weeks from baseline *p<0.05.